REMARKS/ARGUMENTS

Claims 1, 10-12, 23, and 24 are pending in this application. Claims 7-9, 25, and 27 are canceled herein without prejudice. Applicants reserve the right to file one or more continuation, continuation-in-part, or divisional applications towards any canceled subject matter. Claims 1, 10-12, 23 and 24 are amended herein. Basis for these amendments and newly added claims may be found in the specification and claims as originally filed. For example, basis for the amendments in claims 1, 23, and 24 may be found paragraphs [0006] and [0056] and in the Examples, paragraphs [0071] to [0078]; basis for the amendments in claims 10-12 may be found in claims 10-12 as originally filed. No new matter has been added.

Applicants wish to thank the Examiner for the telephonic interview on February 8, 2011 and have taken her comments into consideration in amending the claims. In particular, Applicants discussed the cited art references and proposed claim amendments. Applicants discussed distinguishing features between the prior art and the presently claimed invention. In particular, Applicants proposed filing a Declaration under §1.132 including a statement from one or more inventor as to the surprising results found with administration of invention compounds in the absence of liposomes. Accordingly, the §1.132 Declaration is submitted herewith and the claims have been amended to more particularly claim the invention.

Claim Rejections - 35 U.S.C. §112, First Paragraph

Claims 1, 7-12, 23-25, and 27 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for treating a pathological condition such as retinitis allegedly does not reasonably provide enablement for treatment of other ocular pathological conditions such as macular degeneration or ocular vascularization or proliferation.

While not agreeing with this characterization of the specification and claims, but in order to advance prosecution of this application towards grant of a U.S. patent, the claims have been amended to encompass methods for treating intraocular disease, herpes simplex virus-1 (HSV-1) or cytomegalovirus (CMV) retinitis or other ocular viral infections as found in the specification at paragraph [0056] and in the Examples (e.g., Examples 3-5), paragraphs [0025],[0071] to [0078] and reference 5, page 25). Accordingly, Applicants respectfully request withdrawal of the rejection.

Claim Rejections - 35 U.S.C. §112, Second Paragraph

Claims 1, 7-12, 23-25, and 27 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention.

It is alleged that claims 1 and 25 teach ocular proliferative diseases, which makes these claims indefinite because it is allegedly not clear whether applicant intends to claim ocular cancer diseases such as retinoblastoma (U.S. Patent No. 6,590,086 allegedly teaches retinoblastoma as an ocular proliferative disease).

While not agreeing with this characterization of the claims, but in order to advance prosecution of this application towards grant of a U.S. patent, claim 1 has been amended to encompass methods for treating intraocular disease, herpes simplex virus-1 (HSV-1) or cytomegalovirus (CMV) retinitis or other ocular viral infections, and claim 25 has been canceled. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections - 35 U.S.C. §103(a)

Claims 1, 7-12, 23-25, and 27 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over Cheng (Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6) (hereinafter "Cheng"). Applicants respectfully traverse this rejection.

The U.S. Supreme Court decision in KSR International v. Teleflex Inc. modified the standard for establishing a prima facie case of obviousness. KSR, 550 US 398, 82 USPQ 2d 1385 (2007). Under the KSR rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The 2010 KSR Guidelines Update provides additional guidance in view of decisions by the United States Court of Appeals for the Federal Circuit (Federal Circuit) since KSR. However, familiar lines of argument still apply, including teaching away from the claimed invention by the prior art, lack of a reasonable expectation of success, and unexpected results. Indeed, such arguments may have even taken on added importance in view of the recognition in KSR of a variety of possible rationales. See Federal Register, Vol. 75, No. 169, September 1, 2010, page 53645. Applicants respectfully submit that the Office has not met the burden of establishing a prima facie case of obviousness for the reasons discussed below.

Applicant still maintains that the Office has not provided a prima facie case of obviousness.

The claims as amended distinguish over Cheng by claiming methods for treating intraocular disease, herpes simplex virus-1 (HSV-1) or CMV retinitis or other ocular viral infections by intravitreally injecting a solution of microfluidized particles of HDP-cCDV or microfluidized particles of HDP-P-GCV to the eye, wherein the microfluidized particles of HDP-P-cCDV and the microfluidized particles of HDP-GCV have a volume median diameter of about 4.4 μm, and wherein the method does not use liposomes (discussed in paragraphs [0006] and [0056] of the specification).

As discussed in the specification as filed, particularly in Example 5 at paragraph [0077], it was shown by the inventors that a single intravitreal injection of HDP-GCV (having a mean particle size of 8 to 43 μm) into rabbit eyes prevents HSV-1 infection of the retina for 20 weeks, whereas a single intravitreal injection of GCV provided less than one week of protection (see, Cheng et al. *Invest Ophthalmol Vis Sci.* 2002;43:515-21). In, the specification as filed, particularly in Example 3 at paragraph [0071] to [0072] and Figures 4a and 4b, the inventors found that microfluidization of HDP-P-GCV to a particle size of about 4.4 μm, provides a faster release rate and higher free drug concentration in the upper vitreous (away from the injection site) than does the unmodified HDP-P-GCV, i.e. HDP-P-GCV having a mean particle size of 8 to 43 μm.

Further, the cited reference teaches liposomal formulations of HDP-P-GCV. As discussed on page 1531 and in Table 4 of Cheng, it was found that a single intravitreal injection of the liposomal formulation of HDP-P-GCV into rabbit eyes provided only a 4- to 6-week period of antiviral effect.

Applicants respectfully submit that the 20 week length of duration of the anti-viral effect using the microfluidized version of the compound and the finding that microfluidization to about 4.4 μm provides for a faster release rate and higher free drug concentration in the upper vitreous were unexpected based on the teachings in the cited Cheng reference. In support of the discussion herein, Applicants submit a Declaration under §132 from the inventors, discussing the use of liposomal formulations versus the invention microfluidized particles.

There is no motivation or suggestion in Cheng for delivery in the absence of a liposome since that is the precise point of that reference. Applicants submit that the office has not met its burden of showing a prima facie case of obviousness. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Claim Rejections - 35 U.S.C. §103(a)

Claims 1, 7-12, 23-25, and 27 are rejected under 35 U.S.C. §103(a) as allegedly being obvious over Cheng (Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6) in view of U.S. Patent No. 5,516,522 or U.S. Patent No. 5,098,443. Applicants respectfully disagree.

As discussed above, the pending claims distinguish over Cheng by claiming methods for treating specific ocular diseases by intravitreally injecting a solution of microfluidized particles of HDP-cCDV or microfluidized particles of HDP-P-GCV to the eye, wherein the microfluidized particles of HDP-cCDV and the microfluidized particles of HDP-P-GCV have a volume median diameter of about 4.4 μm, and wherein the method does not use liposomes. Surprisingly, it has been found that the claimed methods provides for a 20 week length of duration of anti-viral effects, and microfluidization to about 4.4 μm provides a faster release rate and higher free drug concentration in the upper vitreous. In contrast, Cheng teaches liposomal formulations of HDP-P-GCV for treating HSV-1 and CMV, wherein a single intravitreal injection provided only a 4- to 6-week period of antiviral effect.

The '522 patent does not cure the defects of Cheng. Instead, this patent teaches biodegradable, porous delivery devices for the controlled release of pharmaceutical agents. These devices, which are hollow tube shaped and closed at both ends, are composed of a mixture of polycaprolactone and a pore-creating agent, and includes channels for the controlled release of the agent from within the hollowed tube. This patent also teaches that these devices may be used intraocularly for the treatment of posterior segment eye diseases. However, the '522 patent does not teach or suggest any methods for treating herpes simplex virus-1 (HSV-1) retinitis as required by the instant claims, which provides for a 20 week length of duration of anti-viral effects and a faster release rate and higher free drug concentration in the upper vitreous.

The addition of the '443 patent cannot cure the defects of Cheng. Instead, this patent teaches biodegradable polymeric C-shaped ring implants for the intraocular and/or intraorbital controlled release of pharmacological agents. The implants may be inserted through incisions in the eye wall or are sutured around the globe of the eye. This patent also teaches that as the polymer biodegrades, the drug contained therein is slowly released. The '443 patent does not teach or suggest any methods for treating herpes simplex virus-1 (HSV-1) retinitis as required by the instant claims, which provides for a 20 week length of duration of anti-viral activity and a faster release rate and higher free drug concentration in the upper vitreous.

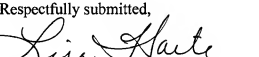
Applicants respectfully submit that the surprising 20 week length of anti-viral effects, provided by the claimed methods, and the finding that microfluidization to about 4.4 μm provides for a faster release rate and higher free drug concentration in the upper vitreous, overcomes the obviousness rejection of the instant claims over Cheng II in view of U.S. Patent No. 5,516,522 or U.S. Patent No. 5,098,443. Accordingly, Applicants request reconsideration and withdrawal of these rejections.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

A Petition for a One-Month Extension of Time under 37 CFR 1.136(a) accompanies this response. The Commissioner is hereby authorized to charge $65.00 as payment for the Petition and One- Month Extension of Time fee to Deposit Account No. 07-1896. No other fee is believed due in connection with the filing of this paper. However, the Commissioner is hereby authorized to charge any other fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,



Date: February 22, 2010

Lisa A. Haile, J.D., Ph.D.
Registration No.: 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER LLP (US)
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO Customer No.: 28213